REMARKS

After entry of the amendment, claims 1, 4, 7, 9-17, and 26-27 are pending of which claim 27 is withdrawn. The subject matter of claims 5 and 8 has been incorporated into claim 1. Claims 2, 5, and 8 have been cancelled without prejudice or disclaimer. The claims have been amended without prejudice and disclaimer and find support *inter alia* in the original claims. The amendments to claim 1 find further support in original claims 5 and 8. No new matter has been added. Applicants respectfully request entry of the above claim amendment as it is believed to put the claims in condition for allowance or, alternatively, in better form for consideration on appeal. Thus, entry under 37 CFR §1.116 is correct.

Finality of the Present Action

Applicants respectfully request that the finality of the present action be withdrawn, because the finality of the present Office Action is inappropriate for at least the following reasons.

The Examiner in the enablement rejection in the Final Office Action cites a new reference, *i.e.* Guo *et al.*, to support the rejection. Pursuant to MPEP § 706.07(a), a second or any subsequent action on the merits in any application will not be made final if it includes a rejection, on newly cited art. Because this is a new reference to support the enablement rejection, the action should not have been made final.

Applicants respectfully request that the finality of the Office Action dated June 23, 2008, be reconsidered and withdrawn.

Because of the finality of the Office Action, the filing of a Request for Continued Examination accompanying this response was necessitated. Should the finality of the action be withdrawn as it should, Applicants request a refund of the fee associated with the filing of the Request for Continued Examination.

Rejections under 35 USC § 112, second paragraph

The Examiner rejected claims 5 and 26 under 35 USC § 112, second paragraph, as being indefinite for the recitation of "negligible reduction." Applicants respectfully traverse. However, to expedite prosecution, the claims have been amended without disclaimer or prejudice. Further claim 5 has been cancelled without disclaimer or prejudice and thus the rejection directed to this claim is moot. The comments below are thus directed to the Examiner's arguments relating to the remaining rejected claims.

The Examiner alleges that the term "negligible" as defined in the specification is well outside any reasonable meaning of "negligible" concluding that Applicants cannot define a term as completely contrary to its standard meaning. Applicants strongly disagree with the Examiner's conclusion and standard used.

As clearly explained in MPEP § 2111.01, an applicant is entitled to be his or her own lexicographer and may rebut the presumption that claim terms are to be given their ordinary and customary meaning by clearly setting forth a definition of the term that is different from its ordinary and customary meaning(s). See *In re Paulsen*, 30 F.3d 1475, 1480, 31 USPQ2d 1671, 1674 (Fed. Cir. 1994) (inventor may define specific terms used to describe invention, but must do so "with reasonable clarity, deliberateness, and precision" and, if done, must "'set out his uncommon definition in some manner within the patent disclosure' so as to give one of ordinary skill in the art notice of the change" in meaning) (quoting *Intellicall, Inc. v. Phonometrics, Inc.*, 952 F.2d 1384, 1387-88, 21 USPQ2d 1383, 1386 (Fed. Cir. 1992)). Furthermore, the Federal Circuit has held that a patentee or applicant may use terms in a manner contrary to or inconsistent with one or more of their ordinary meanings if the written description clearly redefines the terms. *Process Control Corp. v. HydReclaim Corp.*, 190 F.3d 1350, 1357, 52 USPQ2d 1029, 1033 (Fed. Cir. 1999) ("While we have held many times that a patentee can act as his own lexicographer to specifically define terms of a claim contrary to their ordinary meaning," in such a situation the written description must clearly redefine a claim term "so as to put a reasonable competitor or one reasonably skilled in the art on notice that the patentee intended to so redefine that claim term."); MPEP 2173.05(a).

Applicants have clearly presented a definition in the specification of the meaning of the term "negligible reduction" as explained in the Amendment and Reply Under 37 CFR 1.111 dated March 7, 2008. See also specification, p. 45, ll. 14-19; p. 24 l. 34 through p. 25 l. 6. Contrary to the Examiner's assertion, an Applicant can define a claim term contrary to its ordinary meaning based on Federal Circuit case law and the Patent Office's own examination procedures.

Nevertheless, in order to expedite prosecution, the claims have been amended without prejudice or disclaimer and do not recite negligible. The rejection is rendered moot. Accordingly, reconsideration and withdrawal of the rejection is respectfully requested.

Rejections under 35 U.S.C. § 112, first paragraph

Written Description

Claims 1-2, 4, and 7-17 were rejected under 35 U.S.C. § 112, first paragraph, for allegedly failing to comply with the written description requirement. Applicants respectfully disagree. However, to expedite prosecution, the claims have been amended without disclaimer or prejudice. Further claims 2 and 8 have been cancelled without disclaimer or prejudice and thus the rejection directed to these claims is moot. The comments below are thus directed to the Examiner's arguments relating to the remaining rejected claims.

The Examiner acknowledges that the recited species would be representative of the entire genus. See Office Action, p. 4, last sentence. Therefore based on the Examiner's own admission, the written description requirement is met under the correct standard.

Applicants disagree with the standard for written description asserted by the Examiner on pages 5 and 6 of the Office Action, which the Examiner alleges are in the written description guidelines. The Examiner alleges that correlation of structure-function relationship of the claimed genus of protein for successful practice of the invention is required for fulfilling written description requirements (Office Action, p. 5). The Examiner further alleges that "when there is substantial variation within a genus, one must describe a sufficient structure and variety of

species to reflect the representative structure variation within the genus." (Emphasis added). The Examiner has misquoted the Written Description Guidelines. Contrary to the Examiner assertion, the Written Description Guidelines rather state that "when there is substantial variation within a genus, one must describe a sufficient variety of species to reflect the variation within the genus." (See Written Description Guidelines, Appendix A, providing Federal Register, Vol. 66, No. 4, at page 1106, right column, item (2) second paragraph). Contrary to the Examiner's assertion, the Guidelines do not mention the requirement for structure when defining a representative number of species. Rather according to the Guidelines, the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice. *Enzo Biochem, Inc. v. Gen-Probe Inc.*, 323 F.3d 956, 964 (Fed. Cir. 2002) (citing to the "Guidelines for Examination of Patent Applications Under the 35 U.S.C.S. § 112, para. 1 "Written Description" Requirement, 66 Fed. Reg. 1099, 1106 (January 5, 2001)" and agreeing with the Patent Office's standard). Moreover, the Guidelines state that "[d]escription of a representative number of species does not require the description to be of such specificity that it would provide individual support for each species that the genus embraces." (emphasis added; See Written Description Guidelines, Appendix A, providing Federal Register, Vol. 66, No. 4, at page 1106, right column, item (2) second paragraph).

The Examiner further alleges that "[f]or inventions in an unpredictable art, adequate written description of a genus, cannot be achieved by disclosing the structure of small portion of only one species within the genus." (Emphasis added). Contrary to the Examiner's assertion, the Written Description Guidelines state that "[f]or inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus." Contrary to the Examiner's assertion, the guidelines do not mention the requirement for structure, but rather that one disclosed species may not be sufficient under those circumstances. In contrast the present specification discloses at least fourteen actual sequences relating to threonine-degrading proteins of the present claims. (See Amendment and Reply Under 37 CFR 1.111 dated March 7, 2008). The Examiner is thus

requiring a different standard than the standard set forth by the Court of Appeals for the Federal Circuit and by the Patent Office.

The Examiner further alleges that the disclosure solely of functional features coupled with minor structural feature that may or may not be present is insufficient to be representative of the attributes and features of the entire genus. Applicants respectfully disagree that the specification discloses only functional features with minor structural features. Contrary to the Examiner's assertion, the specification discloses at least fourteen actual sequences with references to sequences by GenBank Accession numbers which can be used in the method. The Examiner appears to insist on a structure-function correlation, however this is only one of the alternative ways of meeting the written description requirement, which is not required when the requirement can be fulfilled with description of a representative number of species by actual reduction to practice as is clearly the case here where at least fourteen actual sequences are disclosed. The Examiner has not provided an explanation why fourteen actual sequences would not provide a representative number. See also *In re Marzocchi*, 439 F.2d 220, 224 (CCPA 1971); MPEP § 2163.04 (written description under 35 U.S.C. § 112, first paragraph, is presumed to be adequate, unless or until sufficient evidence or reasoning to the contrary has been presented by the examiner to rebut the presumption).

Furthermore, the Examiner has not addressed why the present methods should be treated any differently than the claims in Example 18 of the previous version of the Written Description Examination Guidelines or Example 16 of the revised version which were found to be adequately described (see details in Amendment and Reply Under 37 CFR 1.111 dated March 7, 2008). The Examiner is requiring a different standard than the standard set forth by the Patent Office.

Nevertheless, in order to expedite prosecution, the claims have been amended without disclaimer or prejudice. The subject matter of claims 5 and 8 has been incorporated into claim 1, and thus also into the claims dependent therefrom. Since claim 5 was not included in the rejection and the subject matter of claim 5 is incorporated into the claims as amended, this rejection is believed to be rendered moot. Reconsideration and withdrawal of the rejection is respectfully requested.

Enablement

Claims 1-2, 4-5, and 7-17 were rejected under 35 U.S.C. § 112, first paragraph, for allegedly lacking an enabling disclosure. Applicants respectfully disagree. However, to expedite prosecution, the claims have been amended without disclaimer or prejudice. Further claims 2, 5, and 8 have been cancelled without disclaimer or prejudice and thus the rejection directed to these claims is moot. The comments below are thus directed to the Examiner's arguments relating to the remaining rejected claims.

The Examiner alleges that the specification provides limited guidance and that producing and testing all possible variants would be undue experimentation. There has never been a requirement that every species encompassed by a claim must be disclosed or exemplified. See *In re Angstadt*, 537 F.2d 498 (CCPA 1976). There is no requirement for Applicants to produce and test all possible variants.

The Examiner further contends that the specification must provide guidance if a large amount of screening is required (see Office Action dated Jun 23, 2008, page 10). The standard for enablement does not turn on whether or not a large amount of screening is required. Under the applicable law, the test for "undue experimentation" is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine. *Ex parte Jackson*, 217 USPQ 804, 807 (1982); *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988). In the present case, the specification provides detailed guidance and teaches in the Examples, the types of routine assay which are employed to confirm activity and additionally a working example showing activity (see previous Amendment and Reply under 37 CFR 1.111 dated March 7, 2008).

The Examiner additionally cites to a new reference Guo *et al.* (hereinafter "Guo") for support of the enablement rejection. The Examiner contends that Guo provides a formula for calculating a percentage of active mutants. From a calculation of potential mutants based on this formula, the Examiner contends that guidance is not provided and that undue experimentation would be required. Applicants strongly disagree with the Examiner interpretation of this

reference. The Examiner provided a formula and indicated that it was from Table 1 of Guo. However, Guo discloses that the components of formula [1] and [2] are solved after experimental determination (see Guo, page 9206, left column, 3rd line following formula [1]). Table 1 provides results using the human DNA repair enzyme 3-methyladenine DNA glycosylate (AAG) and generated three different AAG mutant libraries. From the library with the low degree of mutation having a size of 2×10^5, only 20 mutants were sequenced showing that 1 mutant (5%) had no amino acid changes, 4 mutants (20%) showed one amino acid change, 8 mutants (40%) showed two amino acid changes and 3 mutants (15%) showed four amino acid changes within AAG. Based on the data of the library with the low mutation degree and the 20 mutants which have been sequenced, Guo has extrapolated a so-called *x*-factor of 0.39 (39%) and including all three libraries an average *x* factor of 0.34 (34%). Based thereupon the Examiner alleges that the percentage of random single substitution mutation which inactivates AAG is 34%. But this assumption is not correct since Figure 1 of Guo clearly shows that only 34 out of 299 amino acids of AAG cannot be replaced without loss of activity meaning that 299 minus 34 amino acids can be replaced meaning that at least (299-34)/299 = 91% of single mutations result in mutants which are still active. This result is diametrically opposed to the assumption of the Examiner. Therefore it is not appropriate to cite Guo in the present manner, since these data clearly show that the *x* factor is very individual (directly correlated with the examined protein itself, not transferable to other proteins) and the quality thereof is based on the quality and the number of experiments, number of sequenced mutants, etc. Guo further discloses comparisons with other mutagenesis studies in which mutations were targeted to the catalytic center of enzymes, but where data for the components of the formula were available (see Guo, page 9206, left column, lines 22-25). Further, Guo relates to totally different proteins than those in the present application. Given that the values in the formula cited by the Examiner in the Office Action at page 9 were not derived from experimental determination based on the proteins of the present application and that such values should be derived from experimental data as taught by Guo, Guo is not applicable to the present application. Furthermore a calculation of potential mutants or the number of potential mutants is not relevant, because it is not the quantity of experimentation that is important as long as it is routine. See *Ex parte Jackson* , 217 USPQ 804, 807 (1982); and *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988). As already explained in the present case, the specification provides detailed

guidance and teaches in the Examples, the types of routine assay which are employed to confirm activity and additionally a working example showing activity (see previous Amendment and Reply under 37 CFR 1.111 dated March 7, 2008).

Moreover, regarding the percent identity, the facts are analogous to *Ex parte Sun* (pages 14-16, see attached copy for Examiner's convenience), where the Board of Patent Appeals and Interferences found enablement of a polynucleotide having 80% identity to the coding region of the sequence at issue, when the specification described the chemical structures of a specific polynucleotide and polypeptide it encoded, provided an example of how to screen for activity, indicated important areas of the gene that were conserved and those that could be altered, outlined methods for transfection and transformation of plants, and provided examples of successful expression and transformation. *Ex parte Sun*, Appeal No. 2003-1993, Paper No. 27 (Board of Patent Appeals and Interferences) (see attached copy). Similarly here, the specification has described specific polynucleotide sequences and polypeptides they encoded (claimed sequences SEQ ID NO: 1 and 2), provided examples of how to screen for activity (see Examples 7-9 and 13), provided a common structure for the threonine aldolases and a common structure for the lysine decarboxylases (see for example Figures 1 and 2), provided details on transfection and transformation (Examples 10-12), and provided a working example of successful expression and transformation (Examples 7-9 and 13). Thus, it is well within the level of ordinary skill in the art to prepare the nucleic acid sequences as claimed. Moreover, the specification further teaches in detail how to make variants; calculate the percent identity between the disclosed sequences and variant sequences; and test the variant sequences to determine the claimed activity. Thus, the detailed guidance provided in the present specification and the routine nature of the screening for the claimed activity overcome the unpredictability alleged by the Examiner.

Nevertheless, in order to expedite prosecution, claim 1 has been amended without prejudice and disclaimer. Claim 1 incorporates the subject matter of claim 5 and recites that the nucleotide sequence comprises SEQ ID NO: 1, a nucleotide sequence encoding SEQ ID NO: 2 or a nucleotide sequence encoding an amino acid sequence having 85% percent identity to SEQ ID

NO: 2. The 85% percent identity in the present claims is greater than the percent identity found enabled by the Board in *Ex parte Sun*, thus the claims should likewise be found enabled.

The Examiner further alleges that art teaches to avoid changes of 5% of the structure of SEQ ID NO: 2 (see Office Action dated June 23, 2008, p. 10). Based on the Examiner's own rationale, at least claim 26 which recites 95% percent should therefore be found allowable. Applicants request separate consideration for claim 26.

In view of the detailed description, guidance, working examples, and high level of skill, the specification enables the full scope of the present claims without undue experimentation. On these facts, an analysis under *In re Wands* supports enablement. *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988) (routine screening of hybridomas was not "undue experimentation;" the involved experimentation can be considerable, so long as "routine"). Reconsideration and withdrawal of the rejection is respectfully requested.

Rejections under 35 U.S.C. § 102

The Examiner rejects claims 1-2, 5, 7, 10, and 14-16 under 35 U.S.C. 102(b) as being anticipated by Monschau *et al.* (hereinafter "Monschau"). Applicants respectfully disagree and traverse the rejection. However, to expedite prosecution, the claims have been amended without disclaimer or prejudice. Further claims 2, 5, and 8 have been cancelled without disclaimer or prejudice and thus the rejection directed to these claims is moot.

Applicants respectfully disagree and traverse the rejection. However, in order to expedite prosecution, the claims have been amended without disclaimer or prejudice. The subject matter of claims 5 and 8 has been incorporated into claim 1, and thus also into the claims dependent therefrom. Since claim 8 was not included in the rejection and the subject matter of claim 8 is incorporated into the claims as amended, this rejection is believed to be rendered moot. Because Monschau does not teach every limitation of the claims, Monschau does not anticipate the claims as amended. See *Gechter v. Davidson*, 116 F.3d 1454, 1460 (Fed. Cir. 1997) ("[T]o hold that a prior art reference anticipates a claim, the Board must expressly find that every limitation in the claim was identically shown in the single reference.").

Reconsideration and withdrawal of this rejection is respectfully requested.

Rejections under 35 U.S.C. § 103

Claim 11 is rejected as being obvious under 35 U.S.C. § 103(a) over Monschau. Applicants respectfully traverse and urge reconsideration of the rejection for the following reasons.

The Examiner bears the initial burden of establishing *prima facie* obviousness. See *In re Rijckaert*, 9 F.3d 1531, 1532, 28 USPQ2d 1955, 1956 (Fed. Cir. 1993).

Claims 11, the only claim rejected for obviousness is a dependent claim. In *In re Fine*, 837 F.2d 1071, 1076 (Fed. Cir. 1988), the court held that if an independent claim is nonobvious then any claim dependent therefrom is nonobvious. Because the independent claim is not part of the obviousness rejection, then the claims dependent therefrom are likewise nonobvious. The rejection should be withdrawn for this reason alone.

Further, to support a *prima facie* conclusion of obviousness, the prior art must disclose or suggest all the limitations of the claimed invention. See *In re Lowry*, 32 F.3d 1579, 1582, 32 USPQ2d 1031, 1034 (Fed. Cir. 1994); see also *Ex parte Alexander*, 86 USPQ2d 1120, 1122 (BPAI 2007) (where the Board reversed the obviousness rejection in part because the Examiner had not identified all the elements of the claim).

The Examiner alleges that Monschau teaches a method of producing glycine in a fungal strain *Ashbya gossypii* and overexpressing a gene encoding threonine aldolase which degrade threonine, which is allegedly 99.8% identical to SEQ ID NO: 2 of the present application. Applicants strongly disagree with the Examiner's characterization of Monschau. Monschau describes the cloning, disruption and overexpression of the *A. gossypii* GLY1 gene (Monschau, p. 4283, right column, last paragraph). The gene used for transformation in Monschau is the *A. gossypii* GLY1 gene, which Monschau discloses as having ***88% similarity*** (***not 99.8 % identity*** as alleged by the Examiner) to the threonine aldolase from *S. cerevisiae*. (Monschau, abstract, ll. 1-7). Monschau discloses only the percent similarity but the percent identity between these sequences

is considerably lower than 88%. Further, the transgenic expression of the *A. gossypii* GLY1 gene in *S. cerevisiae* was used only to identify the GLY1 gene of *A. gossypii*. Monschau does not teach or suggest or even mention that the expression of the *A. gossypii* GLY1 gene could be used in a process for the production of methionine, homoserine or lysine. Thus, because Monschau does not disclose or teach all the claim limitations, a *prima facie* case of obviousness has not been established for this additional reason.

The Examiner further alleges that all microorganisms including filamentous fungi inherently produce L-amino acids including methionine, homoserine or lysine. Applicants strongly disagree with the applicability of inherency in the context of the present obviousness rejection or that Monschau inherently teaches or suggests production of methionine, homoserine or lysine or that Monschau teaches or suggests the method as claimed.

It is well established that inherency of missing features/limitations is limited to the context of anticipation under 35 U.S.C. § 102. In other words, obviousness under 35 U.S.C. § 103(a) cannot be established through inherency. Furthermore, inherency may not be established by probabilities or possibilities and "[t]he mere fact that a certain thing *may* result from a given set of circumstances is not sufficient [to establish inherency]." *See In re Rijckaert*, 9 F.3d 1531, 1534 (Fed. Cir. 1993). "That which may be inherent is not necessarily known. Obviousness cannot be predicated on what is unknown," even if the inherency of a certain feature is later established. *Id.* Furthermore, the court in *In re Antonie* found that the prior art did not reveal the property which appellant discovered and, therefore, there was no basis to find obviousness. *In re Antonie*, 559 F.2d 618, 619-620 (CCPA 1977) (The claimed wastewater treatment device had a tank volume to contractor area of 0.12 gal./sq. ft. The court found the invention as a whole was the ratio of 0.12 and its inherent property that the claimed devices maximized treatment capacity regardless of other variables in the devices. The prior art did not recognize that treatment capacity was a function of the tank volume to contractor ratio, and therefore the parameter optimized was not recognized in the art to be a result-effective variable.); *see also In re Shetty*, 566 F.2d 81, 86 (CCPA 1977) and *In re Naylor*, 369 F.2d 765, 768 (CCPA 1966); see also MPEP § 2141.02 V. Because the reference cited by the Examiner does not teach, suggest or even mention a process for production of methionine, homoserine or lysine, there is no basis for

finding obviousness. Moreover, analogous to *In re Antonie*, Monschau did not recognize that expression of the gene influences production of methionine, homoserine, or lysine. For this additional reason, a *prima facie* case of obviousness has not been established.

Nonetheless, in order to expedite prosecution, the claims have been amended without disclaimer or prejudice. The subject matter of claims 5 and 8 has been incorporated into claim 1, and thus also into the claims dependent therefrom. Since claims 5 and 8 were not included in the rejection and the subject matter of claims 5 and 8 are incorporated into the claims as amended, this rejection is believed to be rendered moot. Because Monschau does not disclose or suggest all the limitations of the claimed invention, the Examiner has not met his burden of establishing a *prima facie* case of obviousness.

Reconsideration and withdrawal of the obviousness rejection is respectfully requested.

CONCLUSION

For at least the above reasons, Applicants respectfully request withdrawal of the rejections and allowance of the claims. If any outstanding issues remain, the Examiner is invited to telephone the undersigned at the number given below.

Accompanying this response is a petition for a three-month extension of time to and including December 23, 2008 with the required fee authorization. No further fee is believed due. However, if an additional fee is due, the Director is authorized to charge our Deposit Account No. 03-2775, under Order No. 13195-00006-US from which the undersigned is authorized to draw.

Respectfully submitted,

By

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2004 WL 366287 (Bd.Pat.App. & Interf.)

THIS OPINION WAS NOT WRITTEN FOR PUBLICATION

Board of Patent Appeals and Interferences
Patent and Trademark Office (P.T.O.)

EX PARTE YUETIN SUN, BRIAN R. DILKES, BRIAN A. LARKINS, KEITH S. LOWE, WILLIAM J. GORDON-KAMM AND RICARDO A. DANTE

Appeal

No

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2003

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1993

Application No. 09/470,526

NO DATE REFERENCE AVAILABLE FOR THIS DOCUMENT

Before WILLIAM F. SMITH, MILLS and GRIMES
Administrative Patent Judges
MILLS
Administrative Patent Judge

ON BRIEF

DECISION ON APPEAL

This is a decision on appeal under 35 U.S.C. §134 from the examiner's final rejection of claims 2-11, 31, 33 and 35-36 which are the claims on appeal in this application. Claims 14, 32 and 37 have been allowed.

Claim 31 is illustrative of the claims on appeal and reads as follows:

31. An isolated weel nucleic acid comprising a member selected from the group consisting of:
(a) a polynucleotide that encodes a polypeptide of SEQ ID NO:2.;
(b) a weel polynucleotide having at least 80% identity to the entire coding region of SEQ ID NO:1;
(c) a polynucleotide comprising the coding sequence set forth in SEQ ID NO:1; and

(d) a polynucleotide complementary to a polynucleotide of (a) through (c).

The prior art references relied upon by the examiner are:

Aliguc et al. (Aliguc), "Regulation of *Schizosaccharomyces pombe* Wee1 Tyrosine Kinase," J. Biol. Chem., Vol. 272, pp. 13320-13325 (1997)

Hemerly et al. (Hemerly), "Dominant negative mutants of the Cdc2 kinase uncouple cell division from iterative plant development," The EMBO Journal, Vol. 14, pp. 3925-3936 (1995)

Grounds of Rejection

Claims 2-11, 31, 33 and 35-36 stand rejected under 35 U.S.C. § 112, first paragraph as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the art at the time the application was filed that the inventor had possession of the claimed invention.

Claims 2-11, 31, 33 and 35-36 stand rejected under 35 U.S.C. § 112, first paragraph for lack of enablement.

These rejections are reversed.

DISCUSSION

In reaching our decision in this appeal, we have given consideration to the appellants' specification and claims, to the applied references, and to the respective positions articulated by the appellants and the examiner.

Rather than reiterate the conflicting viewpoints advanced by the examiner and the appellants regarding the noted rejections, we make reference to the examiner's Answer for the examiner's reasoning in support of the rejection, and to the appellants' Brief for the appellants' arguments thereagainst. As a consequence of our review, we make the determinations which follow.

Background

*2 The subject matter of the present application is generally directed to corn plant nucleic acids and their encoded proteins which are involved in cell cycle regulation. Specification, page 4. In particular, the claimed invention is directed to a wee1 homologue from maize, zmwee1, whose activity resembles related protein tyrosine kinases. Specification, page 6. The zmwee1 protein is indicated in the specification to be useful in the genetic engineering of the corn plant to increase maize productivity. Specification, page 3.

More specifically, claim 31 is directed to an isolated wee1 nucleic acid comprising a member selected from the group consisting of: a polynucleotide that encodes a polypeptide of SEQ ID NO:2.; a wee1 polynucleotide having at least 80% identity to the entire coding region of SEQ ID NO:1; a polynucleotide comprising the coding sequence set forth in SEQ ID NO:1; and a polynucleotide complementary to a poly-

nucleotide described above.

According to the prior art, Aligue, Weel tyrosine kinase regulates mitosis by carrying out the inhibitory tyrosine 15 phosphorylation of Cdc2 M-phase inducing kinase. Abstract. The specification confirms this, stating "induced weel overexpression results in phosphorylation of p34 at tyrosine-15 (inactivating p34), effectively blocking the transition from G2 into mitosis." Specification, page 37. The "encoded [weel] protein is an important part of the checkpoint control machinery that regulates $p34^{cdc2}$ activity and it's [sic] participation in the active MPF (maturation promoting factor) complex." Specification, page 36. Weel activity can be stimulated by the CDK2-cyclin A complex, or inhibited by nim1. Specification, page 36.

Description

Claims 2-11, 31, 33 and 35-36 stand rejected under 35 U.S.C. § 112, first paragraph as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the art at the time the application was filed that the inventor had possession of the claimed invention.

The Federal Circuit has discussed the application of the written description requirement of the first paragraph of § 112 to inventions in the field of biotechnology. See University of California v. Eli Lilly and Co., 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). The court explained that

> In claims involving chemical materials, generic formulae usually indicate with specificity what the generic claims encompass. One skilled in the art can distinguish such a formula from others and can identify many of the species that the claims encompass. Accordingly, such a formula is normally an adequate description of the claimed genus ... [H]owever, a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA," without more, is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is.

*3 Id.

The Lilly court also stated that "[a] written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." Id. at 1567, 43 USPQ2d at 1405. Finally, the court addressed the manner by which a genus of cDNAs might be described. "A description of a genus of cDNAs may be achieved by

means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus." Id. at 1568, 43 USPQ2d at 1406.

The Federal Circuit has also addressed the written description requirement in the context of DNA-related inventions. See Enzo Biochem, Inc. v. Gen-Probe Inc., 296 F.3d 1316, 63 USPQ2d 1609 (Fed. Cir. 2002). The Enzo court adopted the standard that "the written description requirement can be met by 'showing that an invention is complete by disclosure of **sufficiently detailed, relevant identifying characteristics** ... i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics.'" [Emphasis added] Id. at 1324, 63 USPQ2d at 1613.

The court in Enzo adopted its standard from the USPTO's Written Description Examination Guidelines. See 296 F.3d at 1324, 63 USPQ2d at 1613 (citing the Guidelines). The Guidelines apply to proteins as well as DNAs.

Finally, it is well-settled that the written description requirement of 35 U.S.C. § 112, first paragraph, can be satisfied without express or explicit disclosure of a later-claimed invention. See, e.g., In re Herschler, 591 F.2d 693, 700, 200 USPQ 711, 717 (CCPA 1979): "The claimed subject matter need not be described in haec verba to satisfy the description requirement. It is not necessary that the application describe the claim limitations exactly, but only so clearly that one having ordinary skill in the pertinent art would recognize from the disclosure that appellants invented processes including those limitations." (citations omitted). See also Purdue Pharma L.P. v. Faulding, Inc., 230 F.3d 1320, 1323, 56 USPQ2d 1481, 1483 (Fed. Cir. 2000) ("In order to satisfy the written description requirement, the disclosure as originally filed does not have to provide in haec verba support for the claimed subject matter at issue.").

*4 We apply the relevant law above to the facts before us. In the present case, the examiner argues that the "specification does not set forth what specific structural or physical features define the claimed isolated nucleic acids and transgenic cells, plants and seeds." Answer, page 4. The examiner argues that one skilled in the art "could not predict the structure and function of isolated nucleic acids comprising a weel polynucleotide having at least 80% identity to the entire coding region of SEQ ID NO:1 or a polynucleotide complementary thereto, or cells, plants and seeds transformed therewith. The physical features of the claimed isolated nucleic acids and transgenic cells, plants, and seeds cannot be ascertained in the absence of information about the functional activities of these nucleic acids. Additionally, the specification does not disclose the effect of incorporating the claimed isolated nucleic acids into the genome of a cell or plant." Id.

We find the examiner's argument that one skilled in the art could not predict the structure and function of isolated nucleic acids comprising a weel to be confusing in the context of a written description rejection, as predictability is not the legal standard or test for such rejections. However, as best we can understand the examiner's argument, the examiner appears to argue that the specification does not describe a weel polynucleotide having at least 80% identity to the entire coding region of SEQ ID NO:1.

The examiner argues that "Applicant's [sic] own specification fails to teach a single representative species with 80% identity and WEE1 function." Answer, page 5.

We do not agree with the examiner that claim 31 lacks written description in the specification and that appellants were not in possession of the claimed invention at the time the application was filed. First, to satisfy the written description requirement it is not necessary that the application describe the claim limitations exactly, but only so clearly that one having ordinary skill in the pertinent art would recognize from the disclosure that appellants invented the claimed subject matter. Thus, we do not find the fact that the specification does not specifically teach the structure of a species with 80% identity and WEE1 function to be dispositive of the written description issue here.

The Enzo court stated that "the written description requirement can be met by 'show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics ... i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics.'" Id. at 1324, 63 USPQ2d at 1613 (emphasis omitted, bracketed material in original).

*5 The specification specifically describes the chemical structures of a polynucleotide that encodes a polypeptide of SEQ ID NO:2 and a polynucleotide comprising the coding sequence set forth in SEQ ID NO:1. The specification also provides an example of how to screen for WEE1 activity, specification, Example 1, pages 33-34 and Example 3. Contrary to the examiner's position, it would reasonably appear that such a description in the specification would constitute sufficiently detailed, relevant identifying characteristics of the claimed subject matter consistent with Enzo (*supra*).

In our view, the examiner has failed to indicate why one of ordinary skill in the art, who is in possession of the very specific chemical structures of a polynucleotide that encodes a polypeptide of SEQ ID NO:2 and a polynucleotide comprising the coding sequence set forth in SEQ ID NO:1, would be unable to recognize, upon reading the disclosure, that appellants invented the claimed subject matter, including homologues sharing structural features with the specifically claimed and disclosed structures.

The examiner relies on Aligue for the teaching that amino acids 363-408 of the 550 amino acid N-terminal regulatory domain of *S. pombe* WEE1 are critical to the function of the regulatory domain. The examiner concludes that because "the functional properties of WEE1 and other proteins reside in specific amino acid residues, changes in these residues could have an effect on WEE1 function."

We agree with appellants that the examiner has not established with a preponderance of the evidence, that the combination of the disclosure of the specific chemical structures of a polynucleotide comprising the coding sequence set forth in SEQ ID NO:1, as well as teachings in the specification on how to test for weel activity and teachings of the areas of the weel gene that can be altered without disturbing substrate recognition are insufficient to describe a weel polynucleotide having at least 80% identity to the entire coding region of SEQ ID NO:1. What is evident from the record is those of ordinary skill in the art were aware that most of the variations in amino acid sequences of WEE1 are in the amino terminus, while the carboxy end of the genes are relatively conserved. Those of skill in the art were also aware that the carboxyl terminus and the central portion of the WEE1 protein from *S. pombe* contain the protein kinase domains and sequence crucial for substrate recognition and catalysis. Thus, those of ordinary skill in the art would have recognized from reading the disclosure that the inventors had invented the isolated weel having the specific nucleotide and amino acid sequences and variations of these sequences with mutations in described specific areas of Weel, while avoiding the introduction of mutations in other regions. This teaching, coupled with the ability to test for functional mutants with the assays provided for in the specification, supports appellants' position that the inventors sufficiently described and were in possession of the invention as claimed, at the time of filing of the patent application.

*6 In our view the examiner has not provided sufficient evidence or analysis to indicate why one of ordinary skill in the art having read the disclosure, would not have been able to recognize that the inventors invented the subject matter within the scope of the claims. The rejection of the claims for lack of written description is reversed.

Enablement

Claims 2-11, 31, 33 and 35-36 stand rejected under 35 U.S.C. § 112, first paragraph for lack of enablement.

It is the examiner's position that the specification is enabling for an isolated weel nucleic acid comprising a polynucleotide encoding SEQ ID NO:2 and a polynucleotide comprising SEQ ID NO:1, but does not reasonably provide enablement for a weel polynucleotide having 80% identity to the coding region of SEQ ID NO:1. Answer, page 6.

Enablement is a legal determination of whether a patent enables one skilled in the art to make and use the claimed invention, Raytheon Co. v. Roper Corp., 724 F.2d

951, 960, 220 USPQ 592, 599 (Fed. Cir. 1983), and is not precluded even if some experimentation is necessary, although the amount of experimentation needed must not be unduly extensive. Atlas Powder Co. v. E.I. Du Pont De Nemours & Co., 750 F.2d 1569, 1576, 224 USPQ 409, 413 (Fed. Cir. 1984); W.L. Gore and Associates v. Garlock, Inc., 721 F.2d 1540, 1556, 220 USPQ 303, 315 (Fed. Cir. 1983). Nothing more than objective enablement is required, and therefore it is irrelevant whether this teaching is provided through broad terminology or illustrative examples. In re Marzocchi, 439 F.2d 220, 223, 169 USPQ 367, 369 (CCPA 1971).

An analysis of whether the claims under appeal are supported by an enabling disclosure requires a determination of whether that disclosure contained sufficient information regarding the subject matter of the appealed claims as to enable one skilled in the pertinent art to make and use the claimed invention. In order to establish a prima facie case of lack of enablement, the examiner has the initial burden to establish a reasonable basis to question the enablement provided for the claimed invention. See In re Wright, 999 F.2d 1557, 1561-62, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993) (examiner must provide a reasonable explanation as to why the scope of protection provided by a claim is not adequately enabled by the disclosure). See also In re Morehouse, 545 F.2d 162, 192 USPQ 29 (CCPA 1976).

The threshold step in resolving this issue is to determine whether the examiner has met his burden of proof by advancing acceptable reasoning inconsistent with enablement. "Factors to be considered by the examiner in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman, [230 USPQ 546, 547 (Bd Pat App Int 1986)]. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims." (footnote omitted). In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404, (Fed. Cir. 1988).

*7 In the present case the examiner provided an analysis of several of the relevant enablement factors on pages 5-9 of the Answer. One of the examiner's primary arguments is that the specification does not disclose any specific structural or functional characteristics of any isolated nucleic acid comprising a polynucleotide having at least 80% identity to the entire coding region of SEQ ID NO:1. Answer, page 7. The examiner also argues that the "specification does not disclose any examples of how to make a transgenic host cell or plant comprising an isolated nucleic acid comprising a polynucleotide having at least 80% identity to the entire coding region of SEQ ID NO:1" or provide "any definitive evidence that introducing any isolated nucleic acid comprising a polynucleotide having at least 80% identity to the entire coding region of SEQ ID NO:1 into a plant will result in an alteration of the plant's phenotype." Id.

The examiner relies on Hemerly to support the position that the transformation of

plant material is unpredictable in view of the disclosure. According to the examiner, Hemerly teaches "the transformation of *Arabidopsis* and tobacco plants with isolated nucleic acids encoding wild-type and mutant Cdc2a cell cycle regulatory proteins". Answer, page 8. Transformation of *Arabidopsis* with wild-type Cdc2a and with a Cdc2a mutant designed to accelerate the cell cycle unexpectedly did not affect the development of transgenic plants. The transformation of *Arabidopsis* and tobacco with a Cdc2a mutant designed to arrest the cell cycle did affect the development of transgenic plants as expected. Id.

The examiner concludes (Id., pages 8-9)

> Given the unpredictability of determining the function of isolated nucleic acids comprising a polynucleotide having at least 80% identity to the entire coding region of SEQ ID NO:1, the unpredictability of altering the phenotype of a plant by transforming it with an isolated nucleic acid of SEQ ID NO:1 or isolated nucleic acids comprising a polynucleotide having at least 80% identity to the entire coding region of SEQ ID NO:1, the absence of guidance in the specification for making and using said nucleic acids and transgenic host cells, plants, and seeds, the lack of working examples, and given the breadth of the claims which encompass multiple polynucleotides having at least 80% identity to the entire coding region of SEQ ID NO:1, it would require undue experimentation by one skilled in the art to make and/or use the claimed invention.

Analysis of the enablement requirement in the present case dovetails with our analysis with respect to the written description requirement. In particular, the specification specifically describes the chemical structures of a polynucleotide that encodes a polypeptide of SEQ ID NO:2 and a polynucleotide comprising the coding sequence set forth in SEQ ID NO:1. The specification also provides an example of how to screen for WEE1 activity, specification, Example 1, pages 33-34 and Example 3. Brief, page 9. In addition, the specification page 3, lines 17-31, "describes the level of skill in the art as well as indicating areas of the weel gene that can be altered without disturbing substrate recognition." Brief, page 7. Moreover, the specification, page 3, states, "Most of the variations in amino acid sequences of WEE1 are in the amino terminus, while the carboxy end of the genes are relatively conserved. The carboxyl terminus and the central portion of the WEE1 protein from *S. pombe* contain the protein kinase domains and sequence crucial for substrate recognition and catalysis."

*8 We agree with appellants that the examiner has not established that the combination of the disclosure of the specific chemical structures of a polynucleotide comprising the coding sequence set forth in SEQ ID NO:1, as well as teachings in the specification on how to test for weel activity and teachings of the areas of the weel gene that can be altered without disturbing substrate recognition are insufficient to enable a weel polynucleotide having at least 80% identity to the entire coding region of SEQ ID NO:1.

Nor has the examiner established that one of ordinary skill in the art having the

chemical structures of a polynucleotide comprising the coding sequence set forth in SEQ ID NO:1 and the ability to test for expression as described in the specification, would be insufficient to transform cells, plants and seeds in view of the success described in the specification. While the examiner relies on Hemerly for the transformation of *Arabidopsis* with wild-type Cdc2a and with a Cdc2a mutant, the examiner has not explained how or why potential unpredictability associated with Cdc2a expression is related to or affects Wee1 expression. Nor is it clear from the examiner's analysis that the examiner has fully considered the state of the art as it relates to the transformation of vectors, seeds and plant cells, as outlined in the specification.

The Patent and Trademark Office Board of Appeals stated:

> The test [for enablement] is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed to enable the determination of how to practice a desired embodiment of the invention claimed.

Ex parte Jackson, 217 USPQ 804, 807 (1982).

In our view, upon reading the disclosure, those of ordinary skill in the art would have been provided a reasonable amount of guidance to make and use a wee1 polynucleotide having at least 80% identity to the entire coding region of SEQ ID NO:1. The specification, pages 27-29 outlines methods for transfection and transformation of cells and the introduction of DNA into plants. The examples of the specification indicate successful expression of zmwee1 in E. coli as evidenced by the successful inhibition of cyclin-dependent protein kinase. Specification, pages 33-34. In view of the successful transformation of cells with the disclosed and claimed specific wee1, we find no evidence or sufficient indicated reason of record why one of ordinary skill in the art would not have had a reasonable expectation of success in transforming cells and plant cells with a wee1 polynucleotide having at least 80% identity to the entire coding region of SEQ ID NO:1 without undue experimentation.

The rejection of the claims for lack of enablement is reversed.

CONCLUSION

*9 The rejection of claims 2-11, 31, 33 and 35-36 under 35 U.S.C. § 112, first paragraph as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the art at the time the application was filed that the inventor had possession of the claimed invention is reversed.

The rejection of claims 2-11, 31, 33 and 35-36 under 35 U.S.C. § 112, first paragraph for lack of enablement is reversed.

No time period for taking any subsequent action in connection with this appeal may

be extended under 37 CFR § 1.136(a).

REVERSED

APPEALS AND INTERFERENCES

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